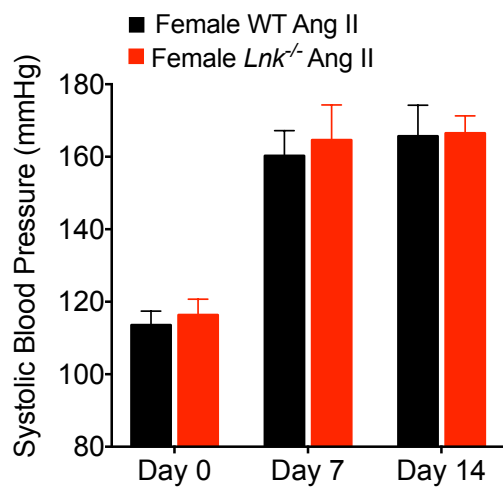
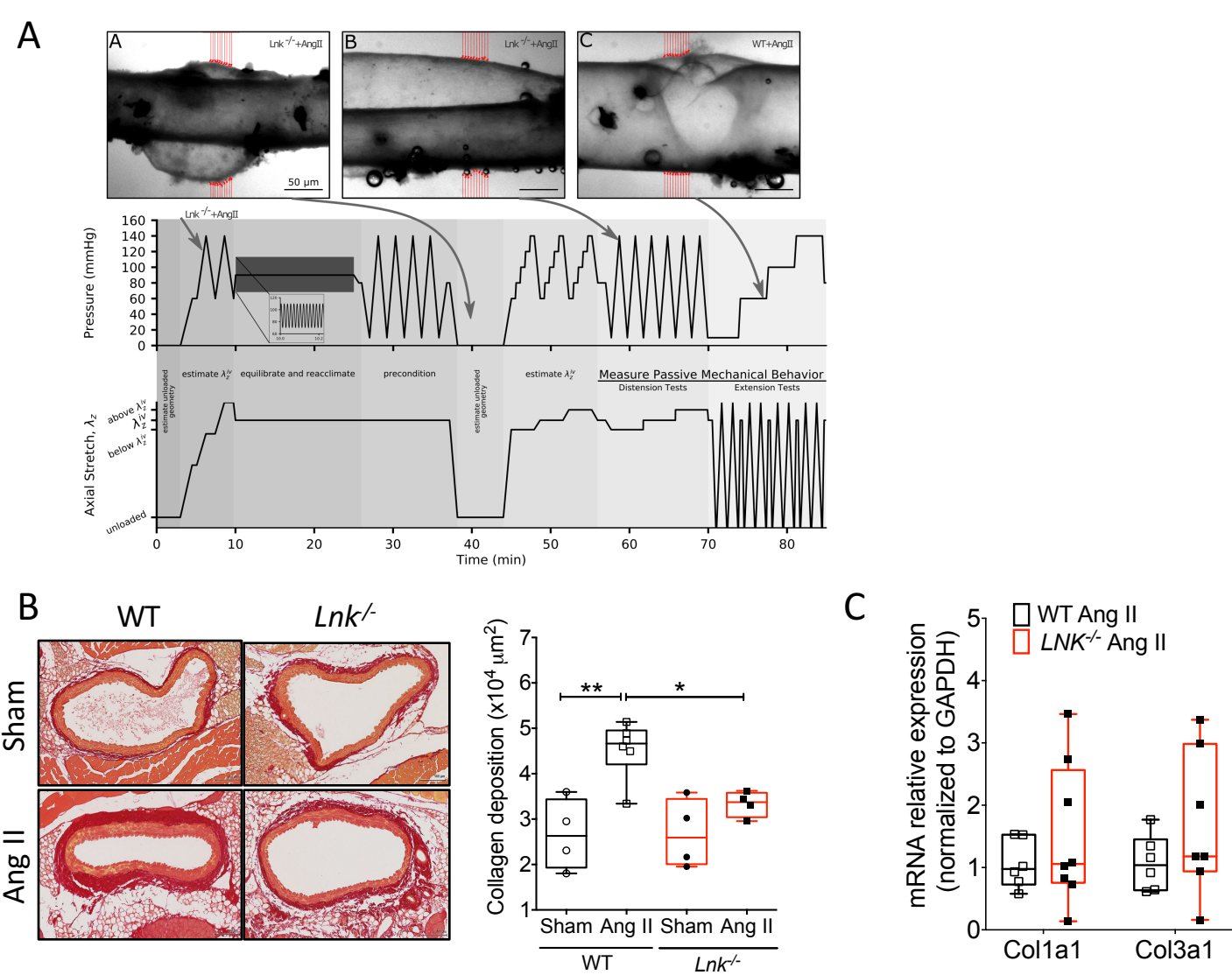


Supplemental Figure 1. *Lnk*^{-/-} mice have similar blood pressure and plasma cholesterol levels compared to WT mice after 14 days of Ang II infusion, but are predisposed to localized aortic inflammation and dissection. (A) Systolic blood pressure measured by telemetry in WT and *Lnk*^{-/-} mice during 14 days of Ang II infusion (n=5-13). (B) Plasma cholesterol concentration in WT and *Lnk*^{-/-} mice infused with Ang II for 14 days (n=4-5). (C) Representative images of immunohistochemical staining for T cells (CD3) and B cells (CD45R) in dissected abdominal aorta of *Lnk*^{-/-} mice. (D) Diameter of the suprarenal abdominal aorta (SAA) between the celiac and superior mesenteric artery of one *Lnk*^{-/-} mouse during 14 days of Ang II infusion as measured by microCT. Example *in vivo* microCT images of the same *Lnk*^{-/-} mouse at days 3, 6, 9, and 12 show localized aggregates of the gold nanoparticles that are thought to be taken up by phagocytic cells and appear white in the SAA as early as day 3. 3-D reconstruction of the SAA at day 13 of Ang II infusion demonstrates localization of the nanoparticles primarily at the celiac and mesenteric artery branches. Data are expressed as mean±SEM (A) or box and whisker plots (B).

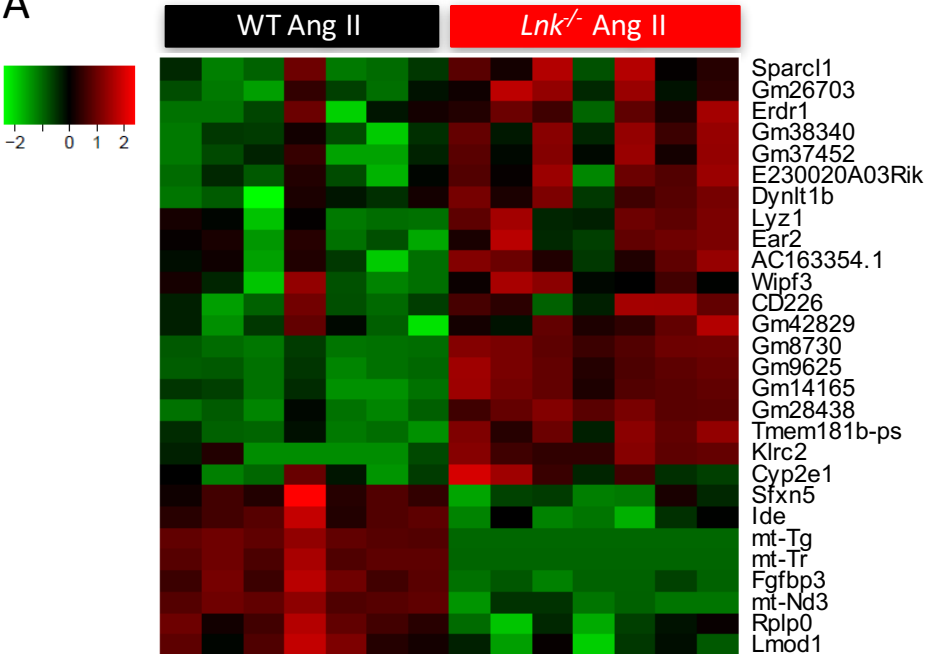


Supplemental Figure 2. Female *Lnk*^{-/-} mice exhibited similar increase in blood pressure compared to female WT mice in response to Ang II infusion. Tail cuff blood pressure in female WT and *Lnk*^{-/-} mice at baseline, day 7, and day 14 of Ang II infusion (n=7-12). Data are expressed as mean±SEM.

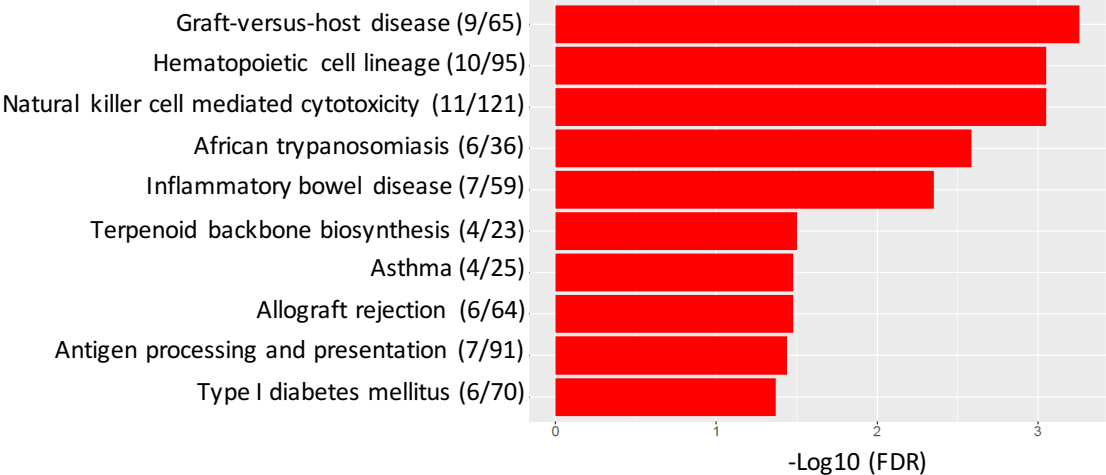


Supplemental Figure 3. LNK deficiency promotes vessel wall vulnerability and early changes in the structural properties of the suprarenal abdominal aorta. (A) SAA from WT and *Lnk*^{-/-} mice treated with Ang II for 3 days were submitted to biaxial mechanical testing. A typical loading protocol is depicted and arrows indicate instances during the protocol where 3 out of 12 SAA from *Lnk*^{-/-} mice and 1 out of 8 SAA from WT mice exhibited mechanical failure. Note that a picture was unable to be obtained for the first *Lnk*^{-/-} mouse as it occurred so quickly. (B) Picrosirius red staining of the abdominal aorta of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days. Representative images are shown on the left, and quantification of collagen deposition is shown on the right (n=4-6). (C) Aortic mRNA expression of the pro-collagens 1a1 and 3a1 (Col1a1, Col3a1) of WT and *Lnk*^{-/-} mice infused for 3 days with Ang II. mRNA expression was normalized to GAPDH and represented as fold change relative to WT Ang II group (n=6-8). Data are expressed as box and whisker plots. **P*<0.05, ***P*<0.01 by 2-way ANOVA.

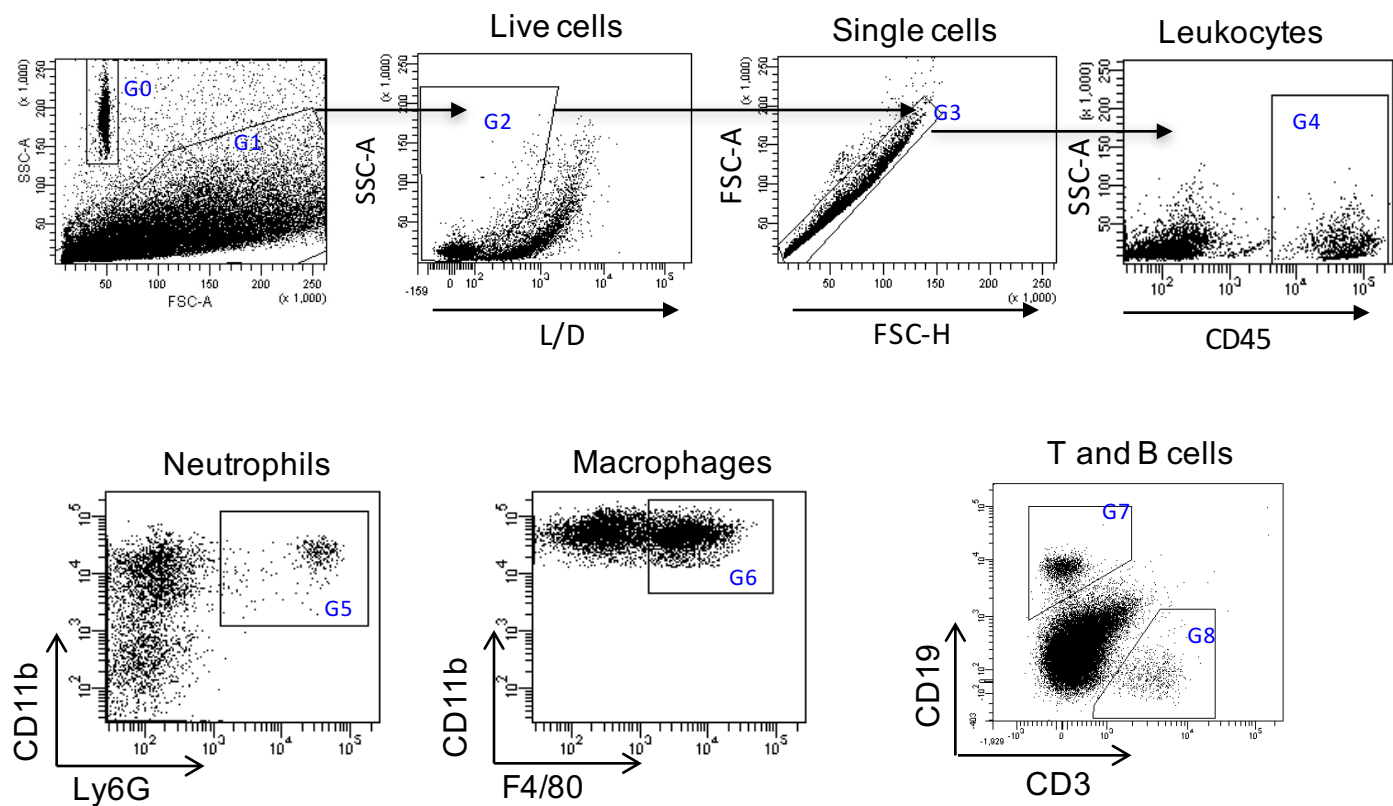
A



B

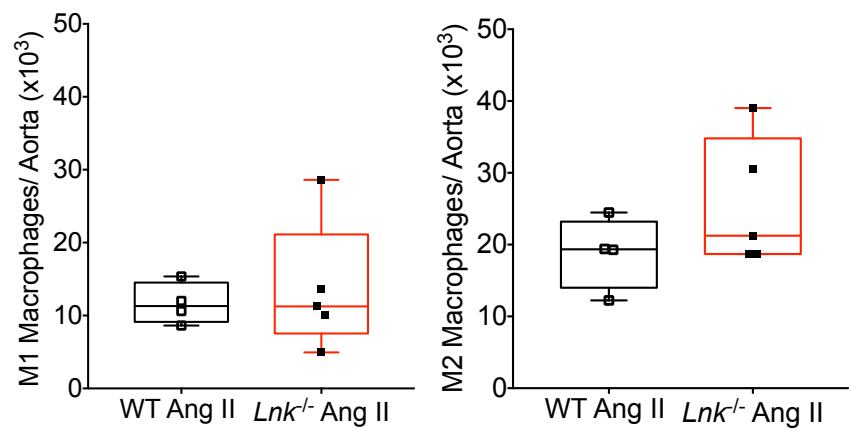


Supplemental Figure 4. RNA sequencing analysis of aortic tissue from WT and *Lnk*^{-/-} mice after 3 days of Ang II infusion demonstrate changes in genes that are enriched in inflammatory pathways. (A) Heat map of the genes differentially expressed between WT and *Lnk*^{-/-} aortas after 3 days of Ang II infusion (adjusted *P* value ≤ 0.05 and absolute fold change ≥ 1.5). (B) KEGG pathway analysis of the differentially expressed genes (*P* value ≤ 0.05 and absolute fold change ≥ 1.5). Top pathways for the differentially expressed genes are shown. FDR=false discovery rate.



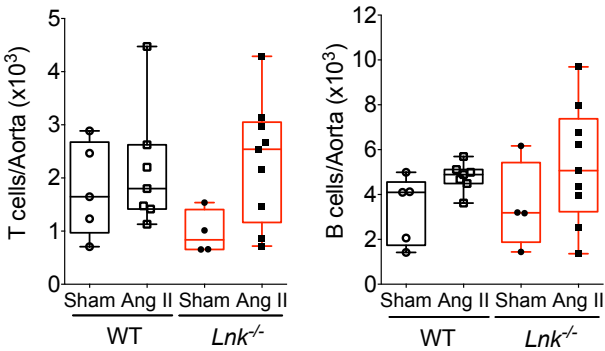
Supplemental Figure 5. Flow cytometry gating strategy to quantify neutrophils, macrophages, T cells, and B cells within the aorta. Cells are first gated (G1) on a forward scatter/side scatter (FSC-A/SSC-A) dot plot and live cells are selected (G2). Cells from G2 are further gated on single cells (G3) and then CD45⁺ leukocytes (G4). From G4, neutrophils are gated on CD11b⁺Ly6G⁺ cells (G5), macrophages on CD11b⁺F4/80⁺ cells (G6), T cells on CD3⁺ cells (G8), and B cells on CD3⁺CD19⁺ cells (G7).

A

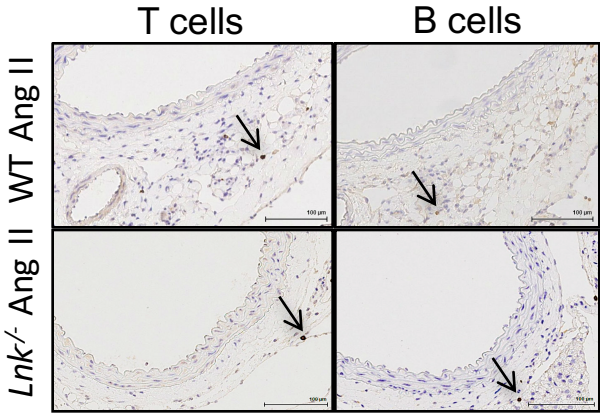


Supplemental Figure 6. WT and *Lnk*^{-/-} mice exhibit the same number of M1 like and M2 like macrophages in the aorta after 3 days of Ang II infusion. Flow cytometric quantification of M1 like macrophages (CD45⁺CD11b⁺F4/80⁺CD206⁻CD80⁺cells) and M2 like macrophages (CD45⁺CD11b⁺F4/80⁺CD206⁺cells) in the aorta of WT and *Lnk*^{-/-} mice infused with Ang II for 3 days (n=4-5). Data are expressed as box and whisker plots.

A

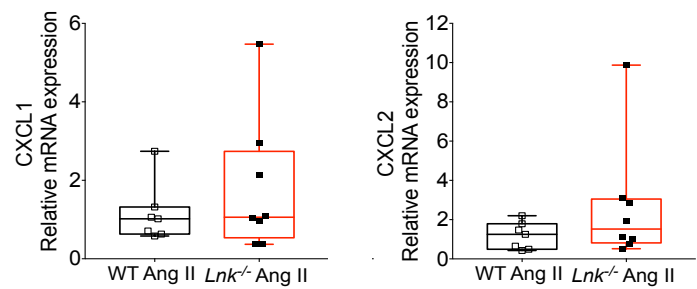


B

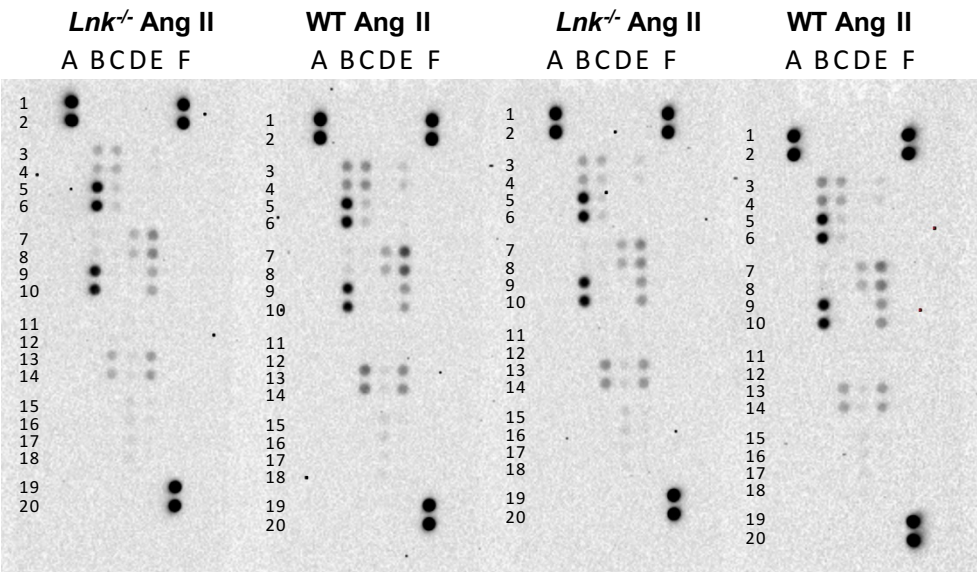


Supplemental Figure 7. Inflammatory cells in the aorta of WT and *Lnk*^{-/-} mice. (A) Flow cytometric quantification of T cells (CD45⁺CD3⁺) and B cells (CD45⁺CD19⁺) in the aorta of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days (n=4-9). (B) Representative images of immunohistochemical staining for T cells (CD3) and B cells (CD45R) in the abdominal aorta of WT and *Lnk*^{-/-} mice infused with Ang II for 3 days. Data are expressed as box and whisker plots (A).

A

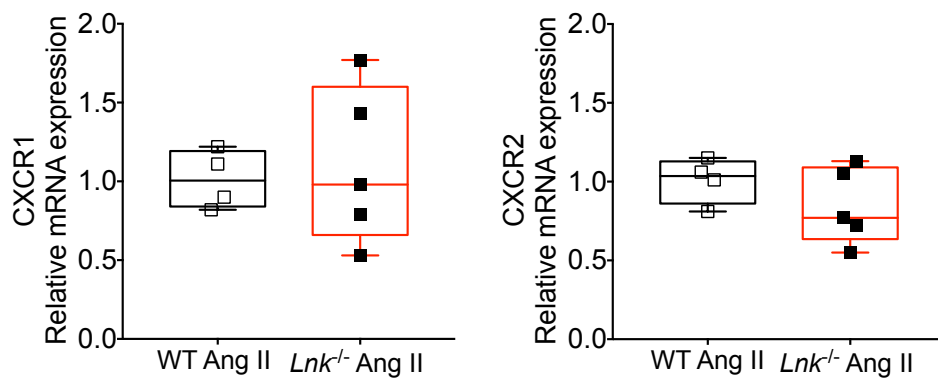


B



Location	Protein	Location	Protein
A1-2	Reference spot	D7-8	IL-16
B3-4	SDF-1	D9-10	IP-10
B5-6	Complement Factor D	D11-12	I-TAC
B7-8	gp130	D13-14	JE
B9-10	HSP60	D15-16	KC
B11-12	Negative control	D17-18	LIX
C3-4	MCP-2	E3-4	CCL21
C5-6	MCP-5	E5-6	CXCL13
C7-8	MDC	E7-8	CCL6
C9-10	MIG	E9-10	Complement Component C5a
C11-12	MIP-1 α/β	E11-12	CCL28
C13-14	MIP-1 γ	E13-14	Chemerin
C15-16	MIP-2	E15-16	CTACK
C17-18	RANTES	E17-18	CXCL16
D3-4	Eotaxin	F1-2	Reference spot
D5-6	Fractalkine	F19-20	Reference spot

Supplemental Figure 8. Expression of aortic chemokines is similar between WT and *Lnk*^{-/-} mice after 3 days of Ang II infusion. (A) Aortic mRNA expression of CXCL1 and CXCL2 from WT and *Lnk*^{-/-} mice infused for 3 days with Ang II. mRNA expression was normalized to GAPDH and represented as fold change relative to WT Ang II group (n=7-8). Data are expressed as box and whisker plots. (B) Chemokine protein array blots of aortic proteins from WT and *Lnk*^{-/-} mice infused with Ang II for 3 days. Analyte identification is shown below for each spot.



Supplemental Figure 9. Neutrophil chemokine receptor CXCR1/2 expression is similar between WT and *Lnk*^{-/-} mice after 3 days of Ang II infusion. mRNA expression of CXCR1 and CXCR2 from neutrophils isolated from the bone marrow of WT and *Lnk*^{-/-} mice infused for 3 days with Ang II. mRNA expression was normalized to GAPDH and represented as fold change relative to WT Ang II group (n=4-5). Data are expressed as box and whisker plots.

Table S1. Morphological and mechanical data for the ascending thoracic aorta (ATA) of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days. Pressure-dependent values were calculated at group-specific systolic pressures (P_{sys}) and axial stretches. Data are expressed as mean±SEM and analyzed by 2-way ANOVA. **P*<0.05, ***P*<0.01 vs corresponding Sham group.

	WT	<i>Lnk</i> ^{-/-}	WT	<i>Lnk</i> ^{-/-}
Parameter	Sham P _{sys} =124 mmHg		Ang II P _{sys} = 151 mmHg	
n	4	4	4	4
Unloaded dimensions				
Outer diameter (µm)	1147±21.27	1176±41.71	1378±93.6	1291±46.97
Wall thickness (µm)	134.6±5.62	157.6±14.16	163±15.68	159.5±8.67
<i>In vitro</i> axial length (mm)	2.575±0.11	2.353±0.14	2.648±0.28	2.49±0.09
Systolic dimensions				
Outer diameter (µm)	1906±11.40	1841±49.58	2267±96.95**	2135±74.61*
Wall thickness (µm)	39±2.45	48.5±5.38	49.5±6.38	47.25±1.93
<i>In vivo</i> axial stretch	1.869±0.04	1.865±0.06	1.827±0.03	1.829±0.03
<i>In vivo</i> circumferential stretch	1.845±0.03	1.763±0.03	1.834±0.05	1.848±0.04
Systolic Cauchy stresses (kPa)				
Circumferential	389.9±24.80	308.7±32.81	458.5±39.71	436±7.10*
Axial	376.4±27.31	344.5±55.79	324.8±47.67	359.8±17.78
Systolic stiffness (MPa)				
Circumferential	3.072±0.38	1.71±0.16	4.986±0.90	4.786±1.22
Axial	2.002±0.24	1.975±0.31	1.834±0.33	1.835±0.18
Systolic stored energy (kPa)	112.5±6.48	99.98±13.48	102.7±19.01	111.7±6.62

Table S2. Morphological and mechanical data for the descending thoracic aorta (DTA) of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days. Pressure-dependent values were calculated at group-specific systolic pressures (Psys) and axial stretches. Data are expressed mean±SEM and analyzed by 2-way ANOVA. **P*<0.05, ***P*<0.01, ****P*<0.001 *****P*<0.0001 vs corresponding Sham group; #*P*<0.05 vs WT Ang II group.

	WT	<i>Lnk</i> ^{-/-}	WT	<i>Lnk</i> ^{-/-}
Parameter	Sham Psys=124 mmHg		Ang II Psys= 151 mmHg	
n	5	4	4	6
Unloaded dimensions				
Outer diameter (µm)	911.20±6.30	896.50±6.77	920.25±2.95	938.33±10.96
Wall thickness (µm)	123.77±1.33	133.15±1.57	130.03±3.26	130.9±2.78
<i>In vitro</i> axial length (mm)	5.95±0.11	4.84±0.19	5.77±0.18	5.17±0.17
Systolic dimensions				
Outer diameter (µm)	1492.15±8.39	1443.44±19.56	1673.23±5.65**	1633.78±18.59**
Wall thickness (µm)	41.61±0.54	45.35±0.43	39.39±1.02	41.46±0.80
<i>In vivo</i> axial stretch	1.62±0.01	1.6±0.01	1.6±0.01	1.6±0.01
<i>In vivo</i> circumferential stretch	1.84±0.02	1.83±0.05	2.07±0.02***	1.97±0.02*, #
Systolic Cauchy stresses (kPa)				
Circumferential	281.12±4.78	246.79±4.01	410.94±11.30****	379.38±6.11****
Axial	261.31±5.61	257.54±6.1	311.38±18.68	328.11±8.64
Systolic stiffness (MPa)				
Circumferential	2.190±0.10	1.503±0.005	3.624±0.34*	2.685±0.15*,#
Axial	3.889±0.08	3.525±0.11	4.709±0.49	5.291±0.90
Systolic stored energy (kPa)	75.47±1.78	70.64±1.79	96.53±3.26*	93.49±2.14*

Table S3. Morphological and mechanical data for the suprarenal abdominal aorta (SAA) of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days. Pressure-dependent values were calculated at group-specific systolic pressures (Psys) and axial stretches. Data are expressed mean±SEM and analyzed by 2-way ANOVA. **P*<0.05, ***P*<0.01, ****P*<0.001 *****P*<0.0001 vs corresponding Sham group; #*P*<0.05, ##*P*<0.01, ###*P*<0.001 vs WT Ang II group.

	WT	<i>Lnk</i> ^{-/-}	WT	<i>Lnk</i> ^{-/-}
Parameter	Sham Psys=124 mmHg		Ang II Psys= 151 mmHg	
n	5	5	8	10
Unloaded dimensions				
Outer diameter (µm)	835.60±12.99	804.20±9.87	878.38±25.43	856.5±23.51
Wall thickness (µm)	113.77±1.88	123.84±4.29	115.03±2.80	121.5±3.73
<i>In vitro</i> axial length (mm)	5.09±0.20	5.13±0.18	6.89±0.34*	5.41±0.49#
Systolic dimensions				
Outer diameter (µm)	1348.53±13.93	1273.86±18.82	1548.85±33**	1394.00±35.95##
Wall thickness (µm)	36.40±0.81	40.07±2.06	35.76±0.66	39.7±1.49
<i>In vivo</i> axial stretch	1.72±0.02	1.71±0.05	1.62±0.02	1.66±0.02
<i>In vivo</i> circumferential stretch	1.82±0.02	1.82±0.05	1.99±0.04*	1.85±0.03##
Systolic Cauchy stresses (kPa)				
Circumferential	290.16±6.09	249.36±15.75	417.29±14.01****	336.60±14.28***, ###
Axial	306.51±4.38	302.54±11.35	350.27±5.31	332.22±3.26
Systolic stiffness (MPa)				
Circumferential	2.073±0.10	1.672±0.07	3.479±0.24****	2.67±0.13**, ##
Axial	3.379±0.09	3.325±0.12	4.787±0.277***	4.351±0.15**
Systolic stored energy (kPa)	78.50±1.44	72.56±5.62	93.1±2.19*	82.26±3.08#

Table S4. Morphological and mechanical data for the infrarenal abdominal aorta (IAA) of WT and *Lnk*^{-/-} mice infused with vehicle (Sham) or Ang II for 3 days. Pressure-dependent values were calculated at group-specific systolic pressures (Psys) and axial stretches. Data are expressed mean±SEM and analyzed by 2-way ANOVA. **P*<0.05, ***P*<0.01 vs corresponding Sham group. §*P*<0.05 vs WT Sham.

	WT	<i>Lnk</i> ^{-/-}	WT	<i>Lnk</i> ^{-/-}
Parameter	Sham Psys=124 mmHg		Ang II Psys= 151 mmHg	
n	4	4	4	6
Unloaded dimensions				
Outer diameter (µm)	556.75±2.11	619.00±4.73§	566.75±8.14	593.5±5.15
Wall thickness (µm)	115.21±1.28	116.49±1.7	117.07±4.23	109.45±2.59
<i>In vitro</i> axial length (mm)	4.82±0.10	4.32±0.38	5.26±0.18	4.42±0.30
Systolic dimensions				
Outer diameter (µm)	869.06±6.74	907.7±7.45	872.84±7.69	905.8±6.16
Wall thickness (µm)	31.13±0.39	37.66±0.95	33.55±0.42	35.1±1.08
<i>In vivo</i> axial stretch	1.95±0.02	1.79±0.03	1.85±0.01	1.75±0.03
<i>In vivo</i> circumferential stretch	1.89±0.04	1.74±0.07	1.88±0.10	1.80±0.03
Systolic Cauchy stresses (kPa)				
Circumferential	214.5±2.55	184.46±5.92	242.15±3.41	245.97±8.08*
Axial	303.08±10.19	265.19±8.91	335.27±2.39	319.14±13.53
Systolic stiffness (MPa)				
Circumferential	1.960±0.05	1.639±0.07	2.38±0.08	2.369±0.08
Axial	3.063±0.05	2.922±0.09	4.814±0.04**	4.663±0.18**
Systolic stored energy (kPa)	61.38±1.07	53.62±2.35	65.28±1.02	62.5±3.11

Table S5. Combination of SNPs with relative weights that predict *SH2B3* gene expression and associate with the AD phenotype.

Position	rsID	Weight	Dosage Allele	Non-Dosage Allele
12:110911239	rs56119242	0.00566	A	G
12:111346382	rs117139109	-0.01543	T	C
12:111344572	rs73195844	0.15327	T	C
12:112161473	rs112310564	0.01734	T	C
12:111343443	rs11065764	-0.02972	C	A
12:111664404	rs3809286	0.00924	T	C
12:111802680	rs7399251	0.10102	T	C
12:111763907	rs188194638	0.07813	T	G
12:111659074	rs4766556	0.09558	C	T
12:111654575	rs7298386	0.08361	G	A
12:111649470	rs112943712	0.09311	G	A
12:111350655	rs3782889	-0.01106	G	A
12:111199943	rs114368233	-0.00606	T	C
12:111231094	rs191621769	-0.03935	C	A
12:111648172	rs73197967	0.14154	G	T
12:111338794	rs11065756	-0.01586	T	C
12:111164920	rs55661717	0.08391	G	A
12:111321724	rs76024719	-0.05582	A	G
12:111165927	rs7132651	0.08352	G	A
12:111798553	rs3742004	0.01730	G	A
12:111335756	rs146280669	-0.01311	G	A
12:111350771	rs3825389	-0.00887	T	C
12:111872722	rs12371484	-0.03377	C	T
12:111657384	rs73197973	0.00888	A	G
12:111651876	rs73197969	0.13782	G	T
12:111331016	rs11065750	-0.01435	A	G
12:111351937	rs11065770	-0.00849	T	C
12:111351186	rs2071629	-0.00945	T	C
12:111331685	rs11065753	-0.01417	T	C
12:111351439	rs11065769	-0.00905	G	T
12:111357471	rs17550549	-0.13053	T	C
12:111350531	rs3782890	-0.01155	A	G